**Retention of triple therapy with methotrexate, sulfasalazine, and hydroxychloroquine compared to combination methotrexate and leflunomide in rheumatoid arthritis, a real world data from the Ontario Best Practices Research Initiative**

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**Objectives:**

1. To assess the retention of triple therapy with methotrexate, sulfasalazine, and hydroxychloroquine compared to combination methotrexate and leflunomide (double therapy).
2. To compare the effectiveness of these treatment strategies at baseline, 6 months, and 12 months after treatment.
3. To investigate the causes of discontinuation of therapy and which agent of the combination was discontinued.

**Methods:**

The inclusion criteria were biologic and JAK inhibitor-naive patients who received triple therapy or double therapy on or after OBRI enrolment between 2008-2022. Baseline characteristics examined included demographics, private health issurance status, smoking use, disease duration, comorbidities, concomitant steroid and NSAID use, lab values, swollen and tender joint counts, physician and patient global assessments, disease activity scores (CDAI, SDAI, DAS28), and HAQ scores.

**Results:**

There were 692 patients included: 258 patients received triple therapy and 434 received double therapy. Statistically significant differences at baseline between the two groups included patients on double therapy being older (58.6 vs 55.3 years), having higher rates of private health issurance (83.2% vs 74.6%), having longer disease duration (8.4 vs 5.8 years), being more likely to have a main comorbidity (43.5% vs 35.7%), and having higher DAS28 scores (mean 4.6 vs 4.3).

Although patients on triple therapy numerically remained on treatment longer, this was not statistically significant. Baseline CDAI scores were similar between the two groups; however, at 6 months, patients on triple therapy were more likely to achieve low-disease activity (42.2% vs 50.7%). Similarly, DAS28 scores were lower at 6 months in patients who received triple therapy (3.4 vs 3.9). Patients on triple therapy were more likely to achieve DAS28 remission at 6 months (30.1% vs 20.3%) and at 12 months (38.4% vs 30.5%).

In multivariable analysis, risk factors for discontinuation of DMARD therapy were being female (HR 1.78) and having a comorbidity (HR 1.27). In patients who received double therapy, leflunomide was stopped more often than methotrexate (220 vs 67 patients). Patients on triple therapy stopped sulfasalazine more often than hydroxychloroquine and methotrexate (96 vs 50 vs 46 patients, respectively).

**Conclusions:**

Although patients on triple therapy numerically remain on treatment longer, this was not statistically significant. Triple therapy was more likely to be associated with reaching low disease activity including

remission at 6 months.  Patients on triple therapy discontinued sulfasalazine more often, and patients on double therapy discontinued leflunomide more often.  Patients who were female and those with at least one comorbidity were more likely to stop therapy